4:45

725-4 Different Effects of Hormone Therapies on Low-Density Lipoprotein Oxidation in Postmenopausal Women

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Considerable experimental evidence suggests that oxidative modification of low-density lipoprotein (LDL) is important in the pathogenesis of atherosclerosis. We have previously shown that 17β-estradiol (E_2) protects LDL from oxidation when administered to postmenopausal women (PMW). In order to assess the antioxidant effect of the more commonly used conjugated estrogen (CE) from equine sources and to assess whether coadministration of progestin interferes with any antioxidant effect of estrogen, we administered CE 0.625 mg daily (30 PMW) or E_2 0.1 mg patch (20 PMW), with and without medroxyprogesterone acetate (MPA) 2.5 mg daily, each therapy for 1 month in a randomized, crossover study. Only CE ± MPA reduced LDL levels and raised high-density lipoprotein (HDL) levels. Neither CE nor CE+MPA prolonged the spectrophotometric time to onset of copper-catalyzed oxidation of LDL (LDLox): (74 ± 9 to 76 ± 10 min, (p = 0.50), and 76 ± 11 to 75 ± 12 min, (p = 0.59), respectively, compared with baseline values (data = mean ± SD). E_2 prolonged the time to LDLox (76 ± 13 to 84 ± 15 min, p = 0.02) without inhibition of this antioxidant effect by the addition of MPA (p = 0.754). There was no correlation between effects of hormone therapies on LDLox and effects on LDL or HDL levels. Thus, in contrast to E_2, equine CE administered to PMW does not alter LDLox, possibly due to weak in vitro antioxidant effects of estrone, the principal estrogen of CE. Progestin did not interfere with CE or E_2 effects on LDLox. Further study is required to assess whether the antioxidant E_2 provides greater cardiovascular protection than CE.

5:00

725-5 The Influence of Serum Vitamin E on Cardiac Risk in Patients with Advanced Coronary Disease: Data from the CHAOS Trial

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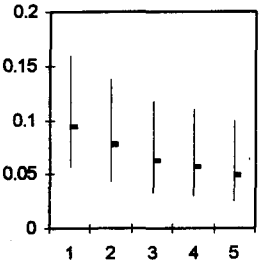
Large doses of Vitamin E reduce the risk of MI in patients with coronary disease. This benefit is probably achieved by inhibition of the oxidation of LDL and the stabilisation of lipid-rich coronary plaques. These doses produce supraphysiological levels of serum α-tocopherol. A related and unresolved issue is whether variations in the endogenous (*unsupplemented*) level of serum α-tocopherol are of sufficient magnitude to also affect cardiac risk. We have examined data from the Cambridge Heart AntiOxidant Study (CHAOS), a clinical trial of Vitamin E in patients with coronary disease, to address this issue.

We studied 855 CHAOS participants on placebo. Fifty four had either nonfatal MI or cardiovascular death during follow-up (median 516 days). There was a reduction in the risk of a cardiac event from the lowest to the highest quintile of serum α-tocopherol. The relative risk (RR) for each rise in quintile was 0.85 (95% CI 0.69–1.03; P = 0.09). The RR between 1st and 5th quintiles of serum level was 0.52 (0.21–1.26; P = 0.19). This trend remained after adjustment for cardiac risk factors and disease severity (RR for each quintile rise 0.83; 95% CI 0.65–1.05; P = 0.12). Odds for each quintile, with 95% CI, are shown.



These data support the concept that endogenous variations in the serum antioxidant α-tocopherol are an important influence on cardiac risk.

5:15

725-6 Elevated Cholesterol in Elderly Survivors of Acute Myocardial Infarction Predicts Reinfarction in the Year after Discharge

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While elevated cholesterol is a risk factor for cardiovascular disease in middle-aged patients, the association in older age remains controversial.

To determine whether cholesterol level was a predictor of recurrent MI among elderly survivors with AMI, we studied 14,168 patients from the Cooperative Cardiovascular Project cohort. These patients were hospitalized with a principal diagnosis of AMI between June 92 and February 93 at one of the 352 non-government acute care hospitals in AL, CT, IA, and WI. Patients with albumin <3 mg/dL or terminal illness were excluded. The final sample comprised 5,475 patients.

After adjusting for demographic and clinical variables, other laboratory results, in-hospital procedures, and discharge medications increasing total cholesterol level had a graded association with an increasing risk of MI readmission in the year after discharge, as shown below. In subgroup analyses, the association persisted in patients >80 years old.

Cholesterol (mg/dL)	RR	95% CI	P value
200–240	1.34	1.02–1.76	0.03
≥240	1.62	1.22–2.15	<0.001

Conclusions: Among elderly survivors of AMI, an elevated cholesterol level is associated with an increased one-year risk for reinfarction.

726 Molecular Biology: Developmental and Genetic Control of Myocardial Structure and Function

Monday, March 17, 1997, 4:00 p.m.–5:30 p.m.
Anaheim Convention Center, Room C2

4:00

726-1 Apoptosis of Muscle Primordia in Somites and Developing Muscle

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Development of the musculoskeletal system involves myogenic determination and differentiation. While myoblast transcriptional maturation has been well characterized, little is known about the molecular mechanisms by which somitic cells decide between cell death and determination/differentiation. Therefore, apoptosis in somites and myoblasts was assessed *in vivo* by TdT-mediated dUTP nick end labeling of mouse embryos and temporally correlated with pro-(Bcl-X_L) and anti-apoptotic (Bax, Bak) gene expression.

TUNEL labeling of embryos at days 8.0 p.c. (somites 1–7) found no evidence of apoptosis outside of the neural tube. However, by day 9.0 p.c., apoptosis was present within somites 1–3 at the rostral end. Thereafter, apoptosis in somites proceeded rostrocaudally in relation to progressive somitic differentiation. At day 9.5 p.c. only somites 1–6, out of the 21–26 somites present at this stage, showed evidence of apoptosis. At the level of the forelimb bud (approximately somites 8–12) many apoptotic cells could be seen. This persisted to at least day 10.5 p.c. Distal to the forelimb bud, several somites continued to manifest apoptotic cells at their rostral end. However, somites caudal to somite 18 were without evidence of apoptosis. Temporal correlation with several pro and anti-apoptotic proteins revealed prominent Bcl-X_L and Bax expression in day E9.5 p.c. somites. At days 12.5–15.5 p.c., Bcl-X_L expression became perinuclear. Myoblasts migrating into the limb bud also expressed Bcl-X_L. Expression of Bcl-X_L decreased markedly after day 14.5 p.c. The relative expression of Bax remained unchanged. This study suggests that apoptosis is present in developing somites and is most apparent at the level of the developing limb where it may allow formation of the appendicular skeleton. The regulation of Bcl-X_L and Bax suggest their regulatory role somitic apoptosis.

MONDAY ORAL